regime. Although data are inconclusive, various agents have been experimented with to provide protection against ANT-induced CMP both in animal models and humans (3,4).

Statins have been shown to decrease atherosclerosis-related morbidity and mortality. It is currently accepted that statins do exert protective cardiovascular effects not solely from their lipid-lowering capacity. In this regard, antioxidative properties are 1 of the main factors by which statins exert so-called pleiotropic effects. Because ANT-induced cardiotoxicity has been shown to be sufficiently triggered by cardiac oxidative stress and inflammation, in the present report it was hypothesized that statins, by their pleiotropic effects, might prevent ANT-induced cardiotoxicity. In a unique animal model, Riad et al. (5) have shown that pretreatment with fluvastatin attenuated ANT-induced CMP. They have demonstrated reduced oxidative stress, enhanced expression of antioxidative enzyme mitochondrial superoxide dismutase 2, and reduced cardiac inflammation shown by decreased tumor necrosis factor-alpha expression in fluvastatin-pretreated mice. They concluded that this outcome resulted from antioxidant and anti-inflammatory effects of fluvastatin.

In the present study, although the inter-group difference on our predefined primary endpoint of LV dysfunction did not reach statistical significance, we have shown that prophylactic use of atorvastatin could be effective in maintenance of LVEF in patients treated with ANT. We proposed that this effect could be related to pleiotropic effects of statins.

The major limitations of the present study are small sample size, lack of placebo group, and the limited measures of cardiac dysfunction that were studied. Also, due to the short follow-up period of the study, late CMP could not be assessed.

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Letters to the Editor

The Israel Screening Failure

Analyzing the Data to Understand the Results

The recent paper by Steinvil et al. (1) raised our concern and prompted the present considerations. The intriguing title conceals the idea that pre-participation screening including 12-lead electrocardiography is ineffective for modifying the occurrence of sudden cardiac deaths (SCDs) in young athletes, in contrast with previously reported Italian data (2).

The authors claim that the yearly incidence of SCDs has remained unchanged (i.e., 2.54 to 2.66 per 100,000 persons) in the periods 1985 to 1996 and 1997 to 2009, despite implementation of the screening program in Israel (1). Their conclusion was that efforts to prevent SCDs in young athletes by the electrocardiographic screening were worthless.

However, we believe that certain methodological limitations do greatly hamper the apparent strength of their conclusion. Primarily, both the number of cardiac events and the population of competitive athletes at risk were only roughly estimated.

First, the number of SCDs was derived only from 2 Israel newspapers, and not from a national prospective registry. Newspapers focus on fatalities occurring in elite/national-level professional athletes, whereas reports of SCDs in the much larger population of adolescents/adults engaged in nonprofessional/regional sports are usually overlooked. Moreover, an increase in the number of sports-related fatal events in more recent years in Western countries has been reported, a phenomenon that simply reflects enhanced public recognition due to increased media attention (3). This may also explain the relative lower prevalence of fatal events reported in the past decades and confirms the unreliability of estimating the time trend of SCDs in athletes based only on media reporting.

Second, the population of competitive athletes at risk is not known. Authors state that the number of registered competitive athletes was 45,000 in 2009. They claim that proportion of Israel population engaged in competitive sports remained unchanged over time, but the actual size doubled, based not on

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national records, but on the U.S. track and field road running records (1).

In conclusion, in this article, the incidence of SCDs was calculated from an uncertain number of events over an estimated number of athletes. The lack of solid numbers for both the numerator and denominator makes the death rates not reliable.

Moreover, we were surprised that results of the Israel screening program were completely ignored: no information was provided regarding the implementation of the national screening, the number of examined athletes, the proportion of disqualified ones, and the cardiac abnormalities discovered. In short, no data derived from the direct experience of sport physicians support the alleged inefficacy of the screening program in Israel.

By comparison, the Italian data were gathered according to a prospective study design with systematic investigation of all young individuals (competitive athletes and sedentary controls) who died suddenly. All of the hearts were examined according to a definite protocol by expert cardiovascular pathologists. Moreover, the number of competitive athletes registered within the athletic sport organizations and undergoing the pre-participation screening program was known for certain. The large diversity of Israel and Italian screening reports make their direct comparison inappropriate.

The Italian experience showed a significant decrease in mortality over the entire time period after the implementation of the screening program (p for trend <0.001), through analysis of the time trend of death rates with Poisson regression of the number of SCDs in each year against the calendar year, including the log of the amount of person-time at risk in each year as an offset term. Poisson regression analysis of the mortality trend over 26 years allowed the potential limitation of a relatively short pre-screening period to be overcome.

Indeed, the comparison of the SCD trend between screened athletes and unscreened nonathletes (i.e., a control population of the same age from the same geographic area) during the same study period provided compelling evidence of the selective decrease in mortality in young athletes undergoing screening.

Although the authors' aim to explain the trend of SCDs in Israel athletes is laudable, their conclusion that the mortality rate in young athletes cannot be changed by implementing pre-participation screening is not supported by scientifically reliable data.

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Media Reporting Bias Affects Reported Sudden Death Rates

Steinvil et al. (1) are to be commended for bringing an important problem into the spotlight. In the past 3 weeks in the United States alone, there have been 5 deaths of student athletes. The current practice of pre-participation history and physical examination does not detect most of the athletes at risk of sudden cardiac death (SCD). However, rather than give us guidance on how to identify high-risk athletes, Steinvil et al. (1) have raised more questions.

First, their study is based on observational data and retrospective analysis, which are appropriate for generating hypotheses but not for drawing significant conclusions or recommending policy changes. Furthermore, the data used were newspaper/media reports, which have inherent limitations and could lead to information bias. For instance, the deaths of less-successful athletes may be under-reported in the media. It is unclear why the authors did not use a more complete source for mortality data, such as the National Center of Forensic Medicine, which was used for a previous similar study in Israel (2).

Furthermore, the deaths reported in this study were only for competitive athletes. The benefit of pre-participation screening may lie among those who engage in physical activity on a noncompetitive level, but such persons were excluded in this analysis. Although Steinvil et al. (1) acknowledged this limitation, they did not estimate its effects. In most populations, this cohort is actually larger than the professional athletes. For instance, in a report on SCD from 1974 to 2002 in the Israel military, there were 74 cases of SCD among Israeli soldiers ages 18 to 39 years (3). These cases were not reported in the media, and yet these cases represent young persons who were engaged in physical activity who died suddenly.

Contrary to what Steinvil et al. (1) reported, the previous large Italian study of SCD in school-age athletes (4) was a prospective study, not a retrospective study, with superior sources of outcomes data. Steinvil et al. (1) concluded that the results of the Italian study were related to a natural variation in SCD incidence rates. However, in the Italian study, incidence rates of SCD were also collected for the unscreened nonathletic young population, and this rate remained constant over the 25 observation years. We think that it is more likely that the marked variation noted in the incidence of SCD in the Steinvil et al. study is due to the source of their data (i.e., that media reporting is related to what is currently in "vogue" and that this reporting may not reflect the true population incidence rate).

We agree with Steinvil et al. (1) that to prevent SCD in this young population, we need to strive for a solution that is feasible and cost-effective. However, we believe that we cannot continue with the status quo. Young athletes continue to die suddenly, and we need to do better with identifying persons at risk. We believe that the solution will require new thinking, and we join the authors in a call for further studies on this serious societal concern.